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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/888,202	07/07/1997	JULIO L. PIMENTEL		1919

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GREG O'BRADOVICH, P.C.
295 CULVER STREET
SUITE A
LAWERENCEVILLE, GA 30045

EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/888,202	PIMENTEL, JULIO L.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1.8.14,18,31,38, 40-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1.8.14,18,31,38, 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.A.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CAR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 30, 2003, is acknowledged and has been entered. An action on the RCE follows.

2 The amendment filed September 30, 2003 is acknowledged and has been entered. Claims 2-4, 7, 11, 17, 19-22, 25-30, 32-37 and 39 have been canceled, claims 1, 14 and 38 have been amended and claims 40-43 have been added. Claims 1, 8, 14, 18, 31, 38 and 40-43 are pending and currently under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Objection

4. Claim 31 is objected to because the claim does not disclose the claim upon which it depends. Because a review of the previous claim set revealed that the claim was dependent upon claim 1 and the omission of the numeral 1 appears to be an inadvertent typographical error, it will be assumed for examination purposes that claim 31 is dependent upon claim 1. Appropriate correction is required.

New Grounds of Rejection

Claim Rejections - 35 USC ' 101

5. 35 U.S.C. ' 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

6. Claims 41-43 are rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility.

The claims are drawn to a method for decreasing fat absorption comprising administering a dosage of an antigen that contains lipase to chickens, optionally administering an additional dosage of the antigen to the chickens, taking a measurement of an antibody titer in the chickens, collecting the antibodies from the chickens, administering the antibodies to an animal and measuring fat absorption of the antibodies in the animal (claim 41), wherein the antigen is swine pancreatic extract (claim 42), wherein the antibodies are collected from the yolks of eggs from the chickens (claim 43).

The specification teaches that antibody to lipase inhibits lipase activity (see Example 4) wherein the effects of anti-lipase antibody are demonstrated in mice wherein total body weight of anti-lipase treated mice was less than that of control animals and wherein it was determined that about 33% more grain was needed to gain 1 gram of body weight in anti-lipase antibody fed mice than control mice (see Example 5). Further, the art teaches that inhibitors of lipase inhibit the digestion of fats (triglycerides) taken in with food wherein food fats are not cleaved and resorption and utilization of these substances is partially prevented and the triglycerides are excreted in unchanged form (US Patent No. 4,598,089, col 3, lines 20-30). However, neither the specification nor the art of record provide guidance on or suggest that the antibodies bind to or absorb fat. In particular, it appears that the fat is excreted in unchanged form. Thus, claims with limitations drawn to the measurement of fat absorption of antibodies are inoperable because it appears that the claimed antibodies do not absorb fat.

Claim Rejections - 35 USC ' 112

7. Claims 41-43 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of a method wherein fat absorption of the antibodies in the mammal is measured has no clear support in the specification and the claims as originally filed. A review of the specification discloses support for measurement of difference in body weight, total feed intake and calculation of grams of feed needed to gain 1 gram of body weight (see examples), however there is no teaching or guidance on measurement of fat absortion of the antibodies in the animal. The subject matter claimed in claims 41-43 broadens the scope of the invention as originally disclosed in the specification.

8. Claims 40 is rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of "the orally fed antibody is fed in an enteric protected form" has no clear support in the specification and the claims as originally filed. A review of the specification discloses support for feeding the antibody in liposomal preparation but no support for the broadly worded claim which reads on all forms of enteric protection. The subject matter claimed in claim 40 broadens the scope of the invention as originally disclosed in the specification.

9. Claims 1, 8, 14, 18, 31, 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 8, 14, 18, 31 are confusing because claim 1 is drawn to "a method for inhibiting lipase in a mammal related to control animals" by orally feeding avian antibodies. The claim is confusing because it is not clear whether the claim limitations are meant to include a control or are simply drawn to a mammal that

has a relationship to control animals. The rejection can be obviated by amending the claim for example to recite "....a mammal, relative to control,.....".

Claims 1, 8, 14, 18, 31, 38 are indefinite because claims 1 and 38 do not contain a positive process step which clearly relates back to the preamble.

Claim 38 is indefinite because claim 38 is missing a critical element, that element being an indication of a subject to be fed.

Claim Rejections - 35 USC § 103

10. Claims 1, 8, 14, 18, 31, 38 are rejected under 35 U.S.C. 103 as being unpatentable over US Patent No. 4,598,089, of record in view of Ohkaru et al (Clin. Chim. Acta (1989) 182:295-300), of record or JP 02150294, of record, US Patent No. 5,585,098, of record, US Patent No. 5,080,895, of record and US Patent No. 5,001,225.

The claims are drawn to a method of inhibiting lipase in a mammal by orally feeding said mammal with an avian antibody that binds lipase in the gastro-intestinal tract of said mammal (claim 1) wherein said avian antibody is produced in avian eggs (claim 8) wherein prior to the step of feeding said avian antibody the antibody is first freeze dried or spray dried (claim 14), wherein the orally fed antibody is fed in a powder form (claim 18), wherein the orally fed antibody is fed in a liquid form (claim 31), a method for decreasing the absorption of fat by orally feeding a chicken antibody against lipase (claim 38).

US Patent No. 4,598,089 teaches methods for treating or preventing obesity by decreasing the absorption of fat in a mammal by oral administration of tetrahydrolipstatin which is an inhibitor of pancreatic lipase (see Abstract). The patent teaches that the digestion of fats (triglycerides) taken in with food is effected in the intestine by pancreatic lipase and by inhibiting pancreatic lipase, food fats are not cleaved and resorption and utilization of these substances is partially

prevented and the triglycerides are excreted in unchanged form (col 3, lines 20-30), clearly leading to decreased absorption of fat in the mammal. The patent further teaches the administration of tetrahydrolipstatin in food, that is orally, to test animals and further demonstrates a great increase in unaltered triglyceride excretion compared to control (col 3, lines 58-col 4 line 2) and claim a method of treating obesity/decreasing absorption of fat in an afflicted mammal comprising administering tetrahydrolipstatin (see claim 9). US Patent No. 4,598,089 teaches as set forth above but does not teach a method of decreasing fat absorption in mammals by feeding an avian antibody that binds lipase thereby inhibiting lipase activity in the gastrointestinal tract wherein said antibody was produced in avian eggs, wherein the antibody is spray dried and orally fed in powder or liquid forms, does not teach antibody fed in enteric form.

Ohkaru et al teach a monoclonal antibody raised against pancreatic lipase which partially inhibits lipase activity (see abstract).

JP 02140294 specifically teaches a monoclonal antibody against pancreatic lipase which hinders lipase activity (see abstract).

US Patent No. 5, 585,098 teaches the successful oral administration of avian antibodies, isolated from chicken egg yolk, raised against bacterium which causes intestinal infectious diseases in calves or piglets which has activity against the antigen and is effective in protection of calves or piglets from attack by the same bacterium in the intestines (col 5, lines 4-17). US Patent No. 5, 585,098 further teaches that although the IgY molecule is disassembled by naturally occurring enzymes in the intestines, it is disassembled into antibody binding fragments which comprise peptides of the highly variable portion of the antibody, Fab fragments (col 7, lines 20-34). US Patent No. 5, 585,098 teaches the advantages of egg yolk antibodies, for example, chicken antibodies do not react with mammalian

complement, Fc receptors, protein A or protein G and show great acid and heat resistance, extraction of yolk antibodies can be performed even on a large scale without costly investment and concentrating the antibody from egg yolk is a relatively straightforward process. Further, the antibody is not harmed by pasteurization and the FDA regards egg antibody as a food rather than a drug and has granted GRAS (generally accepted as safe) status thereto (para bridging cols 1 and 2) and further teaches that the antibodies are in the form of a powder (claims 17 and 18).

US Patent No. 5,080,895 teaches that it is well known in that art that many infectious diseases in livestock can be prevented by oral administration of an antibody against the bacterium which induces the disease (col 3, lines 4-6) and teaches the production of avian egg yolk antibodies wherein a hen is immunized with antigen and four weeks later an additional dosage of antigen is administered, antibody titre is determined, eggs collected and yolks separated and combined together, (see Example I, columns 8 and 9) the egg yolk is stirred or homogenized into an emulsion and spray-dried to form a powder which is recovered as the desired antibody-containing substance. This substance can be orally administered to animals affected by intestinal infectious disease for therapeutical purposes (para bridging columns 3 and 4) and administration of the antibody powder dissolved in artificial milk is exemplified in Example II. These antibodies are particularly beneficial to use in the treatment or prevention of intestinal infections (col 4, lines 62-68). When the antigen used in immunization of the hen is a bacterium which causes intestinal infectious diseases, the avian antibody has activity against the antigen and is therefore effective in protecting animals from attack by the same bacterium in the intestines (col 6, lines 37-42). US Patent No. 5, 585,098

exemplifies the successful administration and use of avian antibodies which are active in the intestinal tract (see Example III, cols 10-11).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce an avian antibody, by the methods of either US Patent No. 5,585,098 or 5,080,895, against the antigen of Ohkaru et al or JP 02140294 to produce antibodies against lipase because US Patent No. 5, 585,098 specifically teaches that chicken egg yolk antibodies are very stable antibodies in that they show great acid and heat resistance and that in addition they do not react with mammalian complement, Fc receptors, protein A or protein G. One would have been motivated to produce an avian antibody against the antigen of Ohkaru et al or JP 02140294 to produce antibodies against lipase because US Patent No. 5, 585,098 specifically teaches that extraction of yolk antibodies can be performed even on a large scale without costly investment and concentrating the antibody from egg yolk is a relatively straightforward process. Further, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to isolate antibodies that inhibit lipase activity in order to further characterize lipase which was known in the art to be important in the process of fat metabolism. One would have a reasonable expectation of success in producing and isolating antibodies that inhibit lipase because both Ohkaru et al and JP 02140294 specifically successfully used their antigens to produce inhibitory antibodies.

Further, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to alter the method of US Patent No. 4,598,089 whereby the avian antibodies of the combined references are substituted for the tetrahydrolipstatin of US Patent No. 4,598,089 and administered by the oral methods of US Patent Nos. 5,585,098 or 5,080,895 (that is in liquid or spray dried

powder form) because the tetrahydrolipstatin of US Patent No. 4,598,089 and the avian antibodies of the combined references have a common mode of administration and a common function, that is the successful inhibition of lipase activity and therefore are functional equivalents. Although no express suggestion that the substitution of the oral antibody for the oral drug be made, the court found in *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982) that an express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. One would have been motivated to substitute the avian antibodies of the combined references for the tetrahydrolipstatin of US Patent No. 4,598,089 in the method of US Patent No. 4, 598,089 because US Patent No. 5, 585,098 specifically teaches the stability of the avian antibodies, their lack of reactivity with mammalian complement, Fc receptors, protein A or protein G and further because US Patent No. 5,585,098 specifically teaches that the FDA regards egg antibody as a food rather than a drug and has granted GRAS (generally accepted as safe) status thereto.

One would have a reasonable expectation of success in achieving anti-lipase activity in the gastrointestinal tract/decreased absorption of fat by substituting the avian antibodies of the combined references for the tetrahydrolipostatin of US Patent No. 4,598,089 in the method of US Patent No. 4,598,089 because both US Patent No 5,585,098 and US Patent No. 5,080,895 teach the successful therapeutic use of avian antibodies that are active in the gastro-intestinal tract of mammals. In particular, US Patent No. 5,080,896 specifically teaches that the orally administered antibodies have activity against antigen in the GI tract and that these antibodies are particularly beneficial to use in the treatment or prevention of intestinal infections. Further, although US Patent No. 5,585,098 specifically

teaches that the IgY molecule is disassembled by naturally occurring enzymes in the intestines, US Patent No. 5,585,098 also specifically teaches that the antibodies are disassembled into antibody binding fragments which comprise peptides of the highly variable portion of the antibody, Fab fragments. It is noted that US Patent No. 5,001,225 teaches that Fab fragments lack the Fc fragment of an antibody, clear more rapidly from circulation and have less nonspecific tissue binding than intact antibody (col 9, lines 22-25) and further teach that Fab fragments may be used as well as the intact antibody in methods of treatment (col 9, lines 26-32). Given the exemplification in US Patent No. 5,080,896 of the effective activity of avian antibodies in the gastrointestinal tract, given the known activity of Fab fragments in *in vivo* treatment, given the equivalence of tetrahydrolipostatin and the antibodies of the combined references, one would clearly have had a reasonable expectation of success and the claimed invention is obvious over the cited references.

Applicant's arguments drawn to the previous rejection under 35 USC 103 are relevant-in-part to the instant rejection.

Applicant reiterates arguments that US Patent No. 4,598,089 teaches only the lipase-blocking agent, tetrahydrolipstatin and not any compound or method that identifies anti-lipase antibodies. The argument has been considered but has not been found persuasive for the reasons previously set forth and for the reasons set forth above combining US Patent 4,598,089 and other references of record.

10. Claims 1, 8, 14, 18, 31, 38, 40 are rejected under 35 U.S.C. 103 as being unpatentable over US Patent No. 4,598,089, of record in view of Ohkaru et al (Clin. Chim. Acta (1989) 182:295-300), of record or JP 02150294, of record, US Patent No. 5,585,098, of record, US Patent No. 5,080,895, of record and US Patent

No. 5,001,225, *Supra* and further in view of Kelly et al (Antimicrobial Agents and Chemotherapy, 1997, 41:236-241.

The claims are drawn to a method of inhibiting lipase in a mammal by orally feeding said mammal with an avian antibody that binds lipase in the gastro-intestinal tract of said mammal (claim 1) wherein said avian antibody is produced in avian eggs (claim 8) wherein prior to the step of feeding said avian antibody the antibody is first freeze dried or spray dried (claim 14), wherein the orally fed antibody is fed in a powder form (claim 18), wherein the orally fed antibody is fed in a liquid form (claim 31), a method for decreasing the absorption of fat by orally feeding a chicken antibody against lipase (claim 38), wherein said orally fed antibody is fed in enteric protected form (40).

The combined references teach as set forth above but do not teach the orally fed antibody fed in enteric protected form.

Kelly et al teaches that in order to be therapeutically active, oral immunoglobulin must survive its passage through the intestinal tract which led the authors to study the gastointestinal stability of orally administered immunoglobulin wherein it was found that administration of the immunoglobulin in enteric capsules resulted in substantially higher concentrations of active antibody that survived passage through the intestinal tract compared to naked antibody forms of oral administration.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have formulated the antibody of the combined references into enteric capsules by the method of Kelly et al for administration in the method of the combined references in order to increase the concentration of active antibody that survived the passage through the intestinal tract. One would have been motivated to have formulated the antibody of the combined references

into enteric capsules by the method of Kelly et al for administration in the method of the combined references because it would be expected that a higher concentration of active antibody would lead to increased inhibition of lipase resulting in additionally decreased absorption of fat.

11. No claims allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Susan Ungar
Primary Patent Examiner
August 4, 2005